Applicant respectfully disagrees and asserts that the examples and methods disclosed in the specification are enabling for, at the least, breast diseases that may be detected using gene markers and related gene marker technology. Nevertheless, in an effort to clarify, Applicant submits new claims 50-69 which include the term "breast cancer" rather than "breast disease". Applicant respectfully submits that the new claims are now in a condition for allowance and requests that this rejection be withdrawn.

Applicant further reminds the Examiner that a protein or nucleic acid marker is useful not only for the direct detection of cancer in a biopsy sample but may also be useful in making a diagnosis or prognosis regarding the patient's disease status. Further, a protein or nucleic acid may not be present in high levels or at all in every tumor. For example, in the case of HER2-neu, only 1/3 of breast cancers overexpress this protein. Thus, in a breast cancer library, a very low level of HER2-neu will be present even though it is a very accurate breast cancer marker. Indeed, HER2-neu is used as a standard breast cancer marker.

Overexpression can be assessed by the well-known technique of immunohistochemistry using an antibody directed against the protein. For breast cancer patients with overexpression of HER-2-neu, treatment with Herceptin, a human-mouse chimeric antibody directed against the protein has therapeutic value. Also, if the gene which codes for HER-2-neu is amplified (multiple copies are present) as detected by the well known techniques of *in situ* hybridization, again the patient will likely respond to Herceptin treatment. However, if the patient does not exhibit an amplified gene or overexpression of the protein, treatment with Herceptin is unlikely to be of benefit.

Similarly, testing for estrogen receptor protein by immunohistochemistry is used as an indicator for treatment with anti-estrogens such as Tamoxifen. Only 2/3 of breast cancer patients express estrogen receptor in their tumors and thus benefit from Tamoxifen therapy. Based on the above, it is clear that the presence or absence of gene products which are expressed in the body is of diagnostic significance for cancer. Thus, the claimed polynucleotides of the present invention exhibit credible utility for several genres of tests well known in the art.

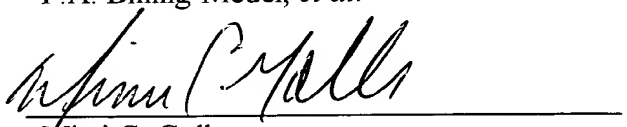
Claims 1-13, 15-16, 33, 35 and 38-49 are further rejected under 35 USC 112, first paragraph because the Examiner states that nowhere in the specification is there a teaching that SEQ ID NO:1-4 encode a mucin. These claims have been canceled. New claims 50-69 do not include this language. In view of the above amendments and remarks, Applicant respectfully submits that new claims 50-69 are in a condition for allowance and requests that this rejection be withdrawn.

Claims 1-13, 15-16, 33, 35, 38-49 are rejected under 35 USC 101 because the claimed invention is not supported by either a specific, substantial or credible asserted utility or a well-established utility. These claims have been canceled. New claims 50-69 further clarify the claimed invention. In view of the above amendments and remarks, Applicant respectfully submits that new claims 50-69 are in a condition for allowance and requests that this rejection be withdrawn.

CONCLUSION

In view of the aforementioned amendments and remarks, Applicant respectfully submits that the above-referenced application is now in a condition for allowance and Applicant respectfully requests that the Examiner withdraw all outstanding objections and rejections and passes the application to allowance.

Respectfully submitted,
P.A. Billing-Medel, *et al.*



Mimi C. Goller
Registration No. 39,046
Attorney for Applicants

ABBOTT LABORATORIES
D-0377/AP6D-2
100 Abbott Park Road
Abbott Park, Illinois 60064-6050
Phone: (847) 935-7550
Fax: (847) 938-2623